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GEORGE BARGER

1878—1939

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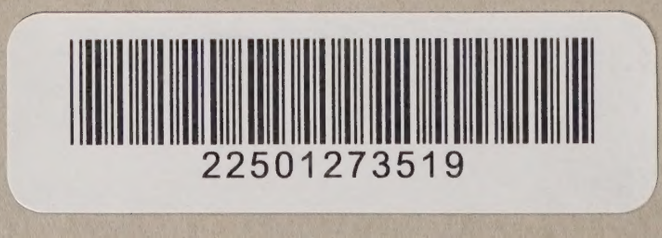

G Barger

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EARLY in January 1939, George Barger, apparently in full health, left home to pay a short visit to friends in Switzerland, and to give a few lectures in the University of Basel. On 6 January came the news of his sudden death from heart failure, at Aeschi, on the Lake of Thun. His early death, not long after his sixtieth birthday, entails a heavy loss to science and to academic life in this country, and a deep personal loss to his many friends here; but there are many men of science in other countries also, who will mourn the loss of a valued friend and colleague, whose wide experience and friendly contacts, with men of so many nationalities and languages, have meant much for the promotion and maintenance of international fellowship in science.

Barger was born in Manchester in 1878; I have known him, indeed, to be proudly insistent on his status as a British subject by birth. His parentage, however, was bi-national, his father Gerrit Barger being a Dutch engineer who had settled for a time in Manchester and married an English wife. While George Barger was yet a child his parents returned to Holland, and there he had his schooling. In a small country like Holland, with a language little spoken or understood beyond its boundaries, the major European languages must, of course, figure prominently in the school curriculum, and be taught to a high standard of accomplishment. Barger, with the additional advantage of having learned to speak in a bilingual home, would undoubtedly be a pupil of unusual aptitude in this and other directions. He must have been precocious, indeed, not only as a learner, but in his power of planning for his own future; for I have heard from him, on one of the rather rare occasions when he spoke of

his boyhood, that the decision for his schooling in Holland to be followed by a university course in England, was taken by himself, with only the acquiescence of his parents. So we find the young Barger at the age of sixteen, coming on his own initiative from his Dutch school, to sit for the Matriculation Examination of the University of London; and with such good result as to be awarded a scholarship which was later to take him to University College, London. Entering University College in 1896, he took a course for the B.Sc. degree, but, before graduating, he had competed for and won an Entrance Scholarship at King's College, Cambridge, where he entered in 1898. I never heard Barger speak much of his short period at University College, but his years at King's, Cambridge, left a very strong impress on his character and habits of mind. He was a little older than most freshmen at entrance, and had behind him an experience widely different from that of the ordinary English schoolboy. Though he was of good physique and vigorous bodily habit, remaining through life a determined and tireless walker on holidays, he had little experience of the conventional English games, and not much aptitude for them. He found himself easily at home, however, and made firm and lasting friendships among a group of contemporaries, most of them with interests widely different from those of his own studies, for whom the late Mr Lowes Dickinson provided a centre of intellectual attraction. I, some years his senior, remember meeting Barger soon after he came to Cambridge. I had no knowledge then of his parentage or history, and the only impression he made on me was that of an unusual undergraduate, with a maturity and a confidence in his own opinions which one did not expect in a freshman.

In 1901 Barger took Part II of the Natural Sciences Tripos, presenting, as then required, a principal and a subsidiary subject. He probably regarded Chemistry as his principal subject and Botany as subsidiary, but, since the examiners placed him in Class I in both, his intention has no more than a conventional interest. I have little doubt, from what he told me in later years,

that he always intended to make Chemistry his life's work, if a suitable opportunity presented itself, though he always kept a lively interest in Botany, the effect of which can be traced in a good part of his chemical work. In any case, the first post which he accepted, after graduating at Cambridge, was as demonstrator of Botany under the late Professor Errera in Brussels. I am sure that he would have regarded this as an opportunity to confirm his fluency in French and perfect his knowledge of that language, while trying his hand at research on some chemical problem with a sufficient botanical interest. The two subjects on which he worked in Brussels continued, in fact, to occupy his interest at intervals for many years after his return to England. The first was the glucoside Saponarin, from *Saponaria*, on which he published his first scientific paper. He became particularly interested in the curious property exhibited by this substance of forming, like starch, a blue compound with iodine; and he recurred at intervals of years, with different co-workers, to the attempt to associate this property with some point of common structure in the substances which exhibit it, the last paper of this widely spaced series being published as late as 1924. In Brussels also he began to work on a comparative method for determining molecular weights on very small quantities of material. The method involved an ingenious and simple application of the well-known phenomenon of isothermal distillation between two solutions of different vapour pressures, and it has been largely superseded. In Barger's own estimation, however, it took a higher rank among his achievements than most others would have accorded to it. It was to him, perhaps, the result of his first really independent enterprise in science, and it had won for him a distinction which he greatly prized—a Fellowship of King's College, Cambridge, which was awarded to him in 1904.

In 1903 Barger accepted appointment as Chemist to the Wellcome Physiological Research Laboratories. This institution had been established some years earlier by Mr Henry S. Wellcome (later Sir Henry S. Wellcome, F.R.S.), the proprietor of Burroughs, Wellcome & Co. The duties of the post which

Barger there accepted were not precisely defined; he was expected to engage in chemical researches, but their scope and direction were not prescribed. He might have turned his attention to the chemistry of bacteria and of immunology, for which the serum-making side of the activities of the Laboratories offered unusual opportunity. His experience and his natural line of interest seemed, however, to lie rather in the direction of plant chemistry, and of substances which could be isolated and identified. He may have received a suggestion, also, that chemical researches with a bearing on the standardization of certain drugs would be regarded with favour. I myself, when I joined the staff of the Laboratories a year later, to conduct researches in pharmacology and physiology, had a clear hint from Mr Wellcome that the obscure pharmacology of ergot in particular might offer a suitable field for my work. I found that Barger, in the year before my arrival, had made experiments on the relation of the known glucosides of digitalis to the activity determined in standardizing that drug on frogs, and had prepared the way for an analogous attack on the ergot problem by making a series of the preparations from ergot which had at that time achieved recognition as "active principles"—sphacelinic acid, chrysotoxin and others. On this basis we started a collaboration which was to last for the next five years. To me it gave a scientific association of inestimable value, and created the bonds of a personal friendship which grew ever closer in the years that followed. It provided for me also the starting-points for almost all the investigations in which I have since been concerned. In Barger's case, I think that it is true to say that it led his interests into fields which he would not have sought spontaneously; for we found ourselves dealing with known substances having physiological activities which had escaped notice, and Barger found himself working on "simpler natural bases", of which the interest was not in their own chemical structure, but chiefly in their occurrence in the animal body, as well as in ergot, or in the physiological effects which they produced on injection.

Early in this joint work we encountered a characteristic

physiological effect which gave direction to the chemical search. After two years of difficult work, Barger, with F. H. Carr, then at the Wellcome Chemical Works, isolated the substance responsible for this action, and found it to be a new alkaloid of ergot, which they named *ergotoxine*. Simultaneously Krafft, in Switzerland, obtained the same substance, and named it *hydroergotinine*. Certainly the new alkaloid was easily convertible into the long-known alkaloid *ergotinine*, which Tanret had isolated in 1879. Krafft believed that the conversion involved the loss of H_2O, and Barger and Carr thought that they had confirmed this relation. It is only in recent years that the change has been recognized as an instance of a curious isomerism, occurring throughout the series of four or five similar pairs of ergot alkaloids which have since been discovered. Ergotinine was, in fact, the first representative of a series of highly dextrorotatory alkaloids, with little or no physiological activity, while ergotoxine was the corresponding first member of the isomeric series, all of which have a low optical rotation and an intense physiological activity. These later developments have been largely due to other workers, but Barger and Ewins had, in 1910, made a first step towards elucidation of the complex structure of ergotoxine, by identifying one of the products of its pyrolytic decomposition as *iso*butyrylformamide.

Ergotoxine accounted for some, but by no means all of the actions of ergot and its extracts. We lacked the clinical control which, thirty years later, enabled Dudley and Moir to isolate ergometrine, though it is strange, even so, that this water-soluble alkaloid was missed, not only by Barger, but by all workers on ergot for so many years. With the guidance only of physiological experiments in the laboratory, Barger tried, for some time without success, to find the substance responsible for a pressor activity, exhibited by ergot extracts in varying degree. Contemporary French work, in which activity of an apparently similar kind had been observed in extracts from putrefying meat, suggested a diversion in that direction. Barger and Walpole soon isolated, from the products of such putrefaction, a series of amines formed

by decarboxylation of amino-acids, of which *isoamylamine* and *tyramine* appeared to be the ones chiefly responsible for the pressor action. Incidentally, this discovery explained an earlier recorded occurrence of a pressor principle in certain extracts of human placenta, from which putrefactive changes had evidently not been excluded. A return to the study of ergot extracts, the large-scale preparation of which was known not to be exempt from putrefaction, showed the presence of the same bases in these. A few years later the search was renewed, in this instance for a substance with an immediate and intense stimulating action on the muscle of the uterus of a cat or a guinea-pig, the activity of which was inhibited by tyramine. When Barger succeeded in isolating the responsible substance, it proved to be the corresponding amine from histidine, soon to be known as *histamine*. The same base had just been isolated by Ackermann, in Germany, from putrefying pancreas, so that a specimen was available to assist the identification.

Barger's concern with these amines did not end with their identification in ergot, though this provided starting-points for much wider developments in physiology and pathology than any in which he himself took part. The actions of isoamylamine and tyramine were found, on more exact analysis, to be largely of the type which we termed 'sympathomimetic', and Barger took responsibility for the chemical planning and conduct of a rather extended study, of a series of compounds intermediate in structure between these simple amines and adrenaline. It was thus possible to observe the stages of approach, in this type of activity, to the intensity and specificity which characterize the action of adrenaline itself, as the type substance and natural hormone of the series. Some years earlier Barger had collaborated in an attempt to find an alternative synthesis for adrenaline, and this experience had familiarized him with compounds of this type, and made it easier for him to fill gaps in the series by devising new syntheses. Most of the recorded observations dealing with histamine, which began with Barger's identification of it as a substance of intense physiological activity, have been

concerned with its biological significance, and its study has given relatively little scope for novel chemical developments. It should not be forgotten, however, that Barger was also the first observer to isolate and identify histamine from a fresh animal tissue. Our choice of intestinal mucous membrane for this demonstration was not, indeed, the most suitable, and the meaning of the result was for some years in doubt; but the more recent preparation of histamine from other normal tissues, free from any suspicion of bacterial contamination, showed that Barger's observation had, in fact, the significance originally accorded to it. Passing mention should also be made, in this connexion, of another substance of striking and specific activity, acetylcholine, the later isolation of which from an ergot extract has played a part in the opening of yet another and more recent chapter in physiology. This identification was, in fact, made after Barger's collaboration in this work had come to an end; but the chemist responsible was A. J. Ewins, who had been Barger's assistant and pupil during the whole of the earlier stages of the work on ergot, and had learned from him, and with him, the details of methods applicable to the isolation of small quantities of unstable substances from such a complex and unpromising mixture.

In 1909 Barger, who was anxious to get a footing in academic work, accepted an appointment as Head of the Department of Chemistry in the Goldsmiths' College, New Cross, though he retained for some years a part-time, consulting connexion with the Wellcome Physiological Research Laboratories. In 1913 he became Professor of Chemistry at the Royal Holloway College, Englefield Green, but this appointment he was not to hold for long. Early in 1914 the Medical Research Committee (now succeeded by the Medical Research Council) had begun to make plans for the appointment of a central research staff, to be housed eventually in a National Institute for Medical Research. I had been invited to become responsible for a department of Biochemistry and Pharmacology, and Barger was approached as to his willingness to join me again as my principal colleague in that department. He asked for, and was readily given, the title

of 'Chemist' on the research staff of the new Institute, and his insistence on such a point was characteristic of his loyal concern for the dignity of his subject. He would willingly serve with, or technically under me, but Chemistry must have its rights of independence in the new Institute, and not be merely subservient to the demands of a programme framed by medical and biological workers. On any terms, I looked forward with eager confidence to the renewal of a personal collaboration which had been so pleasant, and had meant so much for my own work. We took up our new duties together on 1 July 1914. The Medical Research Committee had already acquired the disused hospital building, in Hampstead, which was to house the new Institute, and our first concern was with the fitting of our allotment of rooms as laboratories for our projected department. Having submitted plans for the general lay-out, Barger and I went abroad together, to spend a few weeks visiting the best-equipped laboratories of the Continent and acquiring ideas for the detailed equipment of our own. We came out of Germany only just in time, at the end of the month, and war was declared a few days after we reached England again. Our plans for a programme of normal collaboration had to be abandoned, the building intended for the National Institute becoming, and remaining for the next five years, a military hospital. Barger and I found temporary quarters through the hospitality of the Lister Institute, and there we spent the war years, each absorbed in a series of separate researches and scientific duties which the national need imposed. Barger's record of scientific publication in those years was, of necessity, scanty; but opportunism allowed him occasionally to make a welcome excursion into pure science, from tasks at which he worked with loyal efficiency, but with unconcealed distaste. Such an opportunity produced the elegant little research with F. Tutin which settled the structure of carnosine. Tutin had come to us when invalided from an armament factory, suffering from trinitrotoluene (TNT) poisoning, the nature and irregular incidence of which was one of our preoccupations. Tutin had himself observed that the β and γ

isomers of TNT had the property of condensing with organic bases, like aniline, and the question arose, in connexion with the toxic effects, whether a similar reaction would occur with amino-acids. It was found that it did, and Barger saw the possibility of a condensation between γ TNT and the free amino-group of carnosine, the position of which was then settled by subsequent hydrolysis.

In 1919 Barger accepted the first appointment to a new Chair of Chemistry in Relation to Medicine, in the University of Edinburgh, and held it for the next eighteen years, this being by far his longest continuous tenure of an appointment. The original scheme would have made the Professor responsible for the chemical side of medical education in Edinburgh at all its stages, but there were personal and departmental influences which prevented its realization. For some years Barger found himself restricted in working room, as well as in opportunity, at a time when the new entry of students, just after the war, made an entirely abnormal demand. With the removal of chemistry, apart from the requirements of the medical course, to a new institute outside the city, Barger acquired additional space; but the teaching obligation and opportunity of his department still extended little beyond the elementary needs of the preliminary examination. It was certainly something of an anomaly that a man of his distinction and his capacity for leadership in research should be holding a University Chair, in which he lost sight of his students long before the question of participation in research could arise. Barger, however, became tolerant of a position in which he could find room for the researches of many pupils and colleagues of a maturer type, who soon came to him from other universities of many countries, and which left him freer than most professors and departmental heads, for the visits abroad and the cultivation of personal relations with foreign workers of like interests, which came to play so prominent a part in his life. In 1937 the Regius Professorship of Chemistry in Glasgow fell vacant, and Barger accepted the offer of appointment, with regrets at the severance of pleasant

ties with colleagues in Edinburgh, and at the relinquishment of a post which had given him so much freedom. We may be sure that he would have risen to the full height of the new responsibility, and of an opportunity more worthy of his powers and of his standing in science, if he had lived to enjoy them.

Barger took high rank among British chemists, but he was almost as familiar a figure among physiologists, who were disposed to think of him as chiefly a biochemist. He would not willingly have accepted this description, if it implied the use of chemical methods for the discovery of facts which were biologically, rather than chemically, new and important. Biochemistry has established its claim to recognition as a separate, major field of scientific activity, largely through the activities of those who have built up a special body of technique and a method of approach, in which chemical knowledge, often concerned with known reactions of known substances, is applied to the elucidation of the catalytic systems which characterize vital activity. With such questions of the nature of vital changes, and their intermediate products, Barger's work and interests had little concern. When he became an independent leader, choosing lines of research for himself and his pupils, he seemed to turn naturally to the structural chemistry of such relatively stable end-products of vital activity as the plant alkaloids. As a kind of aftermath of the work on simpler substances, in which the ergot investigation had involved him, he made contact occasionally with work on such compounds as amino-acids and their derivatives; as when, soon after leaving the Wellcome Laboratories, and in collaboration with Ewins who was still there, he showed that the sulphur-containing base, which Tanret had described as 'ergothioneine', was a betaine of thiolhistidine; and when, ten years later, he proved the constitution of the amino-acid, methionine, and, with different pupils, devised two methods of synthesizing it. Even here, however, Barger's contribution to biochemical knowledge was that of the organic chemist dealing with natural products, rather than that of the true biochemist, concerned with the manner of their origin and

their vital significance. A large part of his work, from 1910 onwards, was devoted to relatively complex alkaloids, and established his claim to recognition as one of the leading organic chemists of the country, which came to him fully only towards the end of his life. Ergotoxine was the first alkaloid which he had met in his researches, but he never progressed far in the difficult problem of its structure. With different pupils, he tackled in succession the structure of carpaine, of yohimbine, of physostigmine, of certain alkaloids allied to apomorphine, and of the alkaloids of *Senecio*. As a development of the work on physostigmine with his pupil Stedman, came the synthesis by the latter of simpler but analogous urethanes, of which one at least has acquired therapeutic interest, and the study by the Stedmans of the relation of these substances to cholinesterase. Another justly famous contribution to biochemistry, by one who had been a pupil of Barger, was Harington's elucidation of the structure of thyroxine, and its subsequent synthesis. This work was begun some years after Harington had left Barger's laboratory, but its final stages received so much of Barger's interest in consultation that he was induced to share the authorship of a paper. A more recent example of work begun in collaboration with Barger, and finished in independence by those who had been his pupils, is the work of Todd and his co-workers on the structure and synthesis of 'aneurin' (Vitamin B_1).

Barger was elected to the Fellowship of the Royal Society in 1919, served on the Council from 1930–1932, and was awarded the Davy Medal for 1938, which he received only a month before he left on his last visit to Switzerland. He was for many years an active member of the Chemical Society, serving on its Council from 1913–1917, and as a Vice-President in the year in which he died. He was awarded the Longstaff Medal in 1936, and this and the Davy Medal, since they recognized his services to pure chemistry and his achievements in that science, gave him a particular satisfaction. The Pharmaceutical Society gave him its Hanbury Medal in 1934, which appropriately recognized the importance of some of his work, and particularly that on ergot,

to pharmaceutical chemistry. In 1929 he was President of Section B (Chemistry) of the British Association, which met that year in South Africa. In the previous year he had held a visiting Professorship in Chemistry at Cornell University under the Baker Foundation, and, while in America for that purpose, he delivered the Dohme Lectures at Johns Hopkins University, Baltimore.

Barger had devoted unusual care and study to the preparation of the Dohme Lectures, for which he had chosen "Ergot and Ergotism" as the subject. He had abundant material ready to hand for such a course, requiring only some supplement on the historical side, in dealing with the medieval outbreaks of ergot poisoning in epidemic form. Barger, however, was captured by the interest of the subject, and in the year following the delivery of the lectures he devoted a large part of his time to this historical aspect of the ergot problem, making a number of visits to European libraries in quest of documents and records not easily accessible. As a result, the printed record, of what had begun as a short set of lectures, expanded into a substantial and scholarly monograph. This book on *Ergot and Ergotism* contains, in relatively small compass, a mass of information on so many aspects of its subject that it would have been difficult to find any one else combining the qualities of a direct investigator, a widely trained expert and a cosmopolitan scholar, which went to its production. It provides a better record of the range of Barger's ability and his interests than anything else that he published. Earlier, in 1914, when he retained a closer contact with the work on amines which arose out of his direct investigations on ergot, he had collected into a shorter monograph, on *The Simpler Natural Bases,* information concerning the chemistry and physiological significance of a group of substances not otherwise easily classified. Of a useful rather than original type were a book on *Some Applications of Organic Chemistry to Biology and Medicine*, published in 1930, and a textbook of *Organic Chemistry for Medical Students*, in 1932.

Barger was an honorary graduate of the Universities of Liver-

pool, Padua, Heidelberg, Michigan, Lausanne, and Utrecht, and a number of foreign scientific Academies made him an honorary or corresponding member. He took special pleasure in these recognitions from other countries, but they give but a small indication of the degree to which he became an international figure in science. Multilingual at an early age, from his home and schooling, he continued through life to improve, at every opportunity, his command of the languages he had already, and to add another to his repertoire, whenever the prospect of holiday travel or scientific congress provided the excuse. At physiological gatherings, even more than at those officially concerned with chemistry, he had come to be recognized, semi-officially, as the polyglot spokesman for formal occasions. This facility in many languages, with the more intimate contacts which he made with its help in other countries, enabled him to indulge an interest in alien habits of life and thought. He made more numerous and intimate friendships in other countries than most men do, and his early history favoured a more international outlook on the world than a more conventional training would have done. During the war, especially, when an uncritical nationalism seemed normal, those whose knowledge of Barger was not intimate were sometimes inclined to doubt a patriotism which was less blind and exclusive. Nobody who really knew him, however, could doubt the depth and sincerity of his devotion and his first loyalty to the country of his birth and his later choice; for it was his own unprompted instinct, at the age of sixteen, which had brought him from his father's country back to England, to complete his education and to do his life's work. More, I think, than he himself realized, his effort to understand the point of view of other peoples, and to temper affection for his own with candid criticism, was an essentially English characteristic, which he owed largely to Cambridge and to the circle of his intimates there, though parentage and early experience had made him receptive.

When the war ended, Barger was naturally prominent among those who were eager and active for reconciliation. A fine

opportunity for this came with his appointment as one of the Secretaries to the International Congress of Physiology, which met in Edinburgh in 1923. His unsparing efforts contributed largely to the genuinely international character which the Congress achieved, at a time when a first breach of the barriers was badly needed.

Barger was in thought, as well as in speech and conduct, a man of rigid and determined honesty. Experimental science was his chief concern, and he found no place in it, as a working hypothesis, for any conception but mechanism. His habit of bringing every question to the test of reasoned argument was not a pose, but represented a conscientious effort to achieve a purely rational basis of conduct, and to discard convention and sentiment. In fact there was no man more easily swayed by generous sentiment, or capable of a stronger affection; and, while he seemed sometimes to take trouble to avoid the appearance of complying with unimportant conventions, the standards of a puritan upbringing had more influence than independent theory on his own practice, though not on his lenient judgment of others. He could enjoy a joke concerning his own mild inconsistencies, admitting, for example, the advantages of a tolerant capitalism, which enabled him comfortably to indulge in communist theory without fear of its application. He was, in fact, tolerant and sceptical rather than enthusiastic in politics, but was roused to strong reaction by any threat to justice or to freedom. He understood little of finesse, and sometimes spoke when it would have served his interest better to be silent; but nobody could doubt his candour and sincerity, or his fundamental good feeling.

Barger had a real thirst for experience of all kinds, of which his zest for travel and for encountering new people was one expression. He had a strong historical sense, was moved by great poetry, and had an understanding enjoyment of pictorial art, which he took some pains to practise as an amateur. Chess provided an additional link of common interest with chemical friends in more than one country. More surprising was his apparently

genuine enjoyment of music, in spite of the fact that he was demonstrably tone deaf. He seemed to feel that it was a duty to himself to share in any experience in which any of his friends found rational enjoyment, and his life was full with an unusual variety of interests. He gave and attracted loyalty and steadfastness in friendship with those who won his intimate regard. With his wife, who came of a branch of his mother's family, and the two sons and daughter of their marriage, he had a family life of especially intimate confidence and happiness. Their house in Edinburgh was open in friendly hospitality to his colleagues, pupils and collaborators, and especially to students coming from other countries, or for other reasons outside the normal current of student life.

In many countries of the world there are those who will keep as an inspiration the memory of their association with a great figure in science, who worked with such honest enthusiasm for friendship and understanding, and for the healing of discord.

H. H. DALE

BIBLIOGRAPHY

1902

Saponarin, a new glucoside from Saponaria. *Ber. dtsch. chem. Ges.*, **35**, 1926.

1904

A microscopic method of determining molecular weights. *Trans. Chem. Soc.*, p. 286.

Eine mikroskopische Methode der Molekulargewichtsbestimmung. *Ber. dtsch. chem. Ges.*, **37**, 1754.

(With SHAW, W. V.) The chemical and physiological assay of digitalis tinctures. (Contributed to the Brit. Pharmaceutical Conf. at Sheffield, Aug. 1904, and reprinted from *The Year-Book of Pharmacy*.) *Pharm. J.*, 4 ser., **19**, 249.

1905

Association in mixed solvents. *Trans. Chem. Soc.*, p. 1042.

(With EWINS, A. J.) Application of the microscopic method of molecular weight determination to solvents of high boiling point. *Trans. Chem. Soc.*, p. 1756.

(With JOWETT, H. A. D.) The synthesis of substances allied to epinephrine. *Trans. Chem. Soc.*, p. 967.

1906

Saponarin, a new glucoside, coloured blue with iodine. *Trans. Chem. Soc.*, p. 1210.

(With CARR, F. H.) Note on ergot alkaloids. *Chem. News*, **94**, 89. Abstract of a paper read before the Brit. Assn. (Section B), York Meeting.

(With DALE, H. H.) Die Mutterkornalkaloide. *Arch. Pharmazie*, **244**, 550.

(With EWINS, A. J.) Note on the molecular weight of epinephrine. *Proc. Chem. Soc.*, p. 38.

1907

(With CARR, F. H.) The alkaloids of ergot. *Trans. Chem. Soc.*, p. 337.

(With DALE, H. H.) Ergotoxine and some other constituents of ergot. *Biochem. J.*, **2**, 240.

1908

The action of thionyl chloride and of phosphorus pentachloride on the methylene ethers of catechol derivatives. *Trans. Chem. Soc.*, p. 563.

(With EWINS, A. J.) The action of thionyl chloride on the methylene ethers of catechol derivatives. Part II. Piperonyloin, piperil, and hydropiperoin. *Trans Chem. Soc.*, p. 735.

The action of phosphorus pentachloride on the methylene ethers of catechol derivatives. Part III. The cyclic carbonates of dichloroethyl-y-propylcatechol. *Trans. Chem. Soc.*, p. 2081.

(With EWINS, A. J.) The synthesis of thionaphthen derivatives from styrenes and thionyl chloride. *J. Chem. Soc.*, **93**, 2086.

1909

Isolation and synthesis of *p*-Hydroxyphenylethylamine, an active principle of ergot, soluble in water. *J. Chem. Soc.*, **95**, 1123.

Bemerkung zum Aufsatz von Herrn D. Ackermann: Ueber die Entstehung von Fäulnisbasen. *Hoppe-Seyl. Z.*, **61**, 188.

Constitution of dichloropiperonal. *Ber. dtsch. chem. Ges.*, **42**, 763.

(With DALE, H. H.) The physiological action of primary fatty amines. *J. Physiol.*, **38**, P 22.

(With DALE, H. H.) The water-soluble active principles of ergot. *J. Physiol.*, **38**, P 77.

(With DALE, H. H.) Ueber Mutterkorn. *Arch. exp. Path. Pharm.*, **61**, 113.

(With EWINS, A. J.) The action of phosphorus pentachloride on the methylene ethers of catechol derivatives. Part IV. Derivatives of dihydroxyphenyl-acetic, -glycollic, and -glyoxylic acids. *Trans. Chem. Soc.*, p. 552.

(With WALPOLE, G. S.) Further syntheses of *p*-hydroxyphenyl-ethylamine. *Trans. Chem. Soc.*, p. 1720.

(With WALPOLE, G. S.) Pressor principles from putrid meat. *J. Physiol.*, **38**, P 23.

(With WALPOLE, G. S.) Isolation of the pressor principles of putrid meat. *J. Physiol.*, **38**, 343.

1910

Die Nieuwste Onderzoekingen over Moederkoorn. *Pharm. Weekbl.*, no. 14.

The constitution of carpaine. Part I. *Trans. Chem. Soc.*, p. 466.

(With DALE, H. H.) A third active principle in ergot extracts. Prel. Note. *Proc. Chem. Soc.*, p. 128.

(With DALE, H. H.) The presence in ergot and physiological activity of β-imidazolylethylamine. (Prel. Comm.) *J. Physiol.*, **40**, P 38.

(With DALE, H. H.) 4-β-Aminoethylglyoxamine (β-Iminazolylethylamine) and the other active principles of ergot. *Trans. Chem. Soc.*, p. 2592.

(With DALE, H. H.) Die physiologische Wirkung einer Secalebase und deren Identifizierung als Imidazolyläthylamin. *Zbl. Physiol.*, **24**, 885.

(With DALE, H. H.) Chemical structure and sympathomimetic action of amines. *J. Physiol.*, **41**, 19.

(With EWINS, A. J.) Some phenolic derivatives of β-phenylethylamine. *Trans. Chem. Soc.*, p. 2253.

(With EWINS, A. J.) The alkaloids of ergot. Part II. *Trans. Chem. Soc.*, p. 284.

1911

Bases of bio-chemical interest derived from the proteins. *Sci. Progr. Twent. Cent.*, **6**, 221.

(With DALE, H. H.) β-Iminazolethylamine a depressor constituent of intestinal mucosa. *J. Physiol.*, **41**, 499.

(With EWINS, A. J.) The constitution of ergothioneine: a betaine related to histidine. *Trans. Chem. Soc.*, p. 2336.

(With STARLING, W. W.) β-2-methoxynaphthylpropionic acid and methoxyperinaphthhydrindone. *Trans. Chem. Soc.*, p. 2030.

(With ROMBURGH, P. VAN.) Preparation of the betaine of tryptophan and its identity with the alkaloid hypaphorine. *Trans. Chem. Soc.*, p. 2068.

1912

(With CLARKE, R. W. L.) Oxidation of picrotoxin. *Ber. dtsch. chem. Ges.*, **45**, 3166.

(With FIELD, E.) Blue absorption compounds of iodine. Part I. Starch, saponarin, and cholalic acid. *Trans. Chem. Soc.*, p. 1394.

1913

The chemical pathology of the alimentary tract: the possible pathological significance of putrefaction bases formed in the intestine. *Tr. Int. Congr. Med.*, 1913. Lond. 1914. Sub-sect. III. (a) *Chem. Path.* pt. 2, p. 83.

(With EWINS, A. J.) The identity of trimethylhistidine (histidine-betaine) from various sources. *Biochem. J.*, **7**, 204.

(With STARLING, W. W.) Blue adsorption compounds of iodine. Part II. The influence of constitution on the adsorption by 2- and 4-pyrone derivatives. *Proc. Chem. Soc.*, p. 128.

1914

(With STARLING, W. W.) Blue adsorption compounds of iodine. Part III. Derivatives of 2- and 4-pyrone. *Proc. Chem. Soc.*, p. 303.

The simpler natural bases. Lond. New York etc. Longmans, Green & Co.

(With DALE, H. H.) Liver nitrogen in anaphylaxis. *Biochem. J.*, **8**, 670.

(With STARLING, W. W.) Crystals of organic compounds coloured blue by iodine. *Proc. Chem. Soc.*, p. 2.

1915

Darstellung von physiologisch wirksamen Aminen, welche durch Entkarboxylierung aus Aminosäuren hervorgehen. Abderhalden *Handb. biochem. Arbeitsmethoden*, **8**, 261.

Eine mikroskopische Methode zur Bestimmung des Molekulargewichtes. Abderhalden *Handb. biochem. Arbeitsmethoden*, **8**, 1.

(With DALE, H. H.) Note on a supposed soluble toxin, produced in artificial culture by the bacillus of malignant oedema. *Brit. med. J.*, ii, 808.
(With FIELD, E.) Yohimbine (quebrachine). *Trans. Chem. Soc.*, p. 1025.
(With FIELD, E.) The oxidation of aconitine. *Trans. Chem. Soc.*, p. 231.

1916

(With DAKIN, H. D.) Note on some experiments with glyoxaline derivatives. *Biochem. J.*, **10**, 376.

1917

(With DALE, H. H. and DURHAM, F. M.) "Collosol" cocaine. *Lancet*, 1 Dec., p. 825.
(With EWINS, A. J.) Synthesis of γ-2-methyltryptophan. *Biochem. J.*, **11**, 58.

1918

Synthesis of 3:4-dihydroxyphenathrene (morphol) and of 3:4-phenanthraquinone. *Trans. Chem. Soc.*, p. 213.
Poisons and drugs of animal origin. *J. Soc. chem. Ind.*, **37**, 32T.
(With EWINS, A. J.) The supposed formation of ergotoxine ethyl ester from ergotinine. A correction. *Trans. Chem. Soc.*, p. 235.
(With TUTIN, F.) Carnosine, constitution and synthesis. *Biochem. J.*, **12**, 402.
Fine chemicals, medicinal substances and essential oils. *Ann. Rep. Soc. chem. Ind.*, p. 430.

1919

The relation of chemistry to medicine. Inaugural Address to the class of medical chemistry. *Edinb. med. J.*, n.s. **23**, 350.
Physiological Chemistry. *Chem. Soc. Ann. Rep.*, **16**.

1920

Ergot: its history and chemistry. Inaugural Sessional Address delivered before the Evening Meeting of the North British Branch of the Pharmaceutical Society, November 19.
Physiological Chemistry. *Chem. Soc. Ann. Rep.*, **17**.

1923

Report on the investigations to protect timber against teredo. *Third (Interim) Rept. Comm. Inst. Civil Eng.* (on deterioration of structures in sea-water), p. 24.

The active principles of the pituitary body. *Prescriber,* **17,** 189.

(With STEDMAN, E.) Physostigmine. I. Alkylation products of eseroline. *J. Chem. Soc.,* **123,** 758.

(With WHITE, F. D.) The constitution of galegine. *Biochem. J.,* **17,** 827.

(With WHITE, F. D.) Galuteolin, a new glucoside from *Galega officinalis. Biochem. J.,* **17,** 836.

1924

Report on biological work on the effect of poisons on *Teredo.* *Fourth (Interim) Rept. Comm. Inst. Civil Eng.* (on deterioration of structures in sea-water), p. 23.

(With EATON, F. J.) Blue adsorption compounds of iodine. Part IV. *Trans. Chem. Soc.,* p. 2407.

1925

(With STEDMAN, E.) Physostigmine (Eserine). III. *J. Chem. Soc.,* **127,** 247.

1926

Deterioration of (timber) structures in sea-water. Experimental work of F. D. White and C. M. Yonge at Plymouth during July and August 1924. *Sixth (Interim) Rept. Comm. Inst. Civ. Eng.* Dept. Sci. Industr. Res., pp. 9–13.

(With STEWART, C. P.) β-Iminazolyl-4 (or 5)-pyruvic acid. *J. Pharmacol.,* **29,** 223.

1927

The thyroid gland and thyroxine. Inaugural Sessional Address delivered before an Evening Meeting in Edinburgh on 18 Nov. 1927, of the Pharmaceutical Soc. of Gt. Britain. *Pharm. J.,* **119,** 609.

Die Hormone. *Z. ärztl. Fortbild.,* **24,** 681.

(With HARINGTON, C. R.) Chemistry of thyroxine. III. Constitution and synthesis of thyroxine. *Biochem. J.,* **21,** 169.

1928

Zur Geschichte des Mutterkorns. *Arch. exp. Path. Pharm.,* **138,** 105.

Die Chemie der Hormone. *Ergebn. Physiol.,* **27,** 780.

Eine mikroskopische Methode zur Bestimmung des Molekulargewichtes. Abderhalden *Handb. biol. Arbeitsmethoden.* Abt. III: Physikalisch-chemische Methoden. Teil A, I. *Hälfte,* p. 729.

Neures über die Chemie der Hormone (90. Versamml. der Gesellsch. deutsch. Naturforsch. u. Aerzte. Beilage zur Klin. Wschr. Nr. 47). *Klin. Wschr.*, **7**, 940 ; also, *Naturwissenschaften*, **16**, 940.

(With COYNE, F. P.) On non-cystine sulphur in proteins. *Arch. Sci. biol.*, **12**, 141.

(With COYNE, F. P.) The amino-acid methionine: constitution and synthesis. *Biochem. J.*, **22**, 1417.

(With SILBERSCHMIDT, R.) The constitution of laurotetanine. *J. Chem. Soc.*, p. 2919.

1929

(With ROBINSON, R.) Attempts to find new anti-malarials. Introduction. *J. Chem. Soc.*, p. 2947.

1930

Some applications of organic chemistry to biology and medicine. New York. McGraw-Hill Book Co. 1930.

1931

Ergot and Ergotism. A Monograph. Based on the Dohme Lectures delivered in Johns Hopkins University, Baltimore, Lond. Gurney & Jackson. 1931.

(With GIRARDET, A.) Constitution de la pukatéine et de la lauréline. *Helv. chim. Acta.*, **14**, 481.

(With WEICHSELBAUM, T. E.). A new synthesis of methionine. *Biochem. J.*, **25**, 997.

1932

Organic chemistry for medical students. Lond. Gurney & Jackson. 1932. 2nd ed. 1936. Spanish translation, 1935.

(With SCHLITTLER, E.) Synthese von l-Pukatein-methyläther. *Helv. chim. Acta.*, **15**, 381.

1933

Ergot and ergotism. *Pharm. J.*, **131**, 597.

(With EISENBRAND, J., EISENBRAND, L. and SCHLITTLER, E.) Die Konstitution des Laurotetanins. *Ber. dtsch. chem. Ges.*, **66**, 450.

(With GIRARDET, A. and ROBINSON, R.) Constitution of Carpaine. Part II. *Helv. chim. Acta.*, **16**, 90.

(With SCHOLZ, C.) Yohimbine (Quebrachine). Part IV. Harman, a degradation product. *J. Chem. Soc.*, p. 614.

(With SCHOLZ, C.) Ueber Yohimbin. *Helv. chim. Acta*, **16**, 1343.

1934

Isoquinoline and other alkaloids. IX Congreso Internac. d. Quimica Pura Aplicada, Madrid. 5–11 April, **9**, IV, 97.

(With DORRER, O.) Chemical properties of puberulic acid, $C_8H_6O_6$, and a yellow acid, $C_8H_4O_6$. *Biochem. J.*, **28**, 11.

(With VON EULER, H. and WILLSTAETTER, R.) Hormonas, vitaminas, fermentos. (Ciclos de Conferencias Pronunciadas en la Universidad Internacional de Verano, en Santander, en el Curso de 1931, Revisadas y puestas al dia por sus autores. Madrid, 1934.)

1935

La thyroxine. *Bruxelles-Méd.*, **16**, 284.

(With BERGEL, F. and TODD, A. R.) Ueber das Thiochrom aus Vitamin B_1 (Antineurin). *Ber. dtsch. chem. Ges.*, **68**, 2257.

(With BERGEL, F. and TODD, A. R.) A crystalline fluorescent dehydrogenation product from vitamin B_1. *Nature*, **136**, 259.

(With SESHADRI, T. R., WATT, H. E. and YABUTA, T.) Alkaloids of Senecio. Part I. Retrorsine. *J. Chem. Soc.*, p. 11.

1936

From physostigmine to prostigmin. *Festschrift Emil Barell*, p. 7.

Las vitaminas. *La Farmacia moderna*, **47**, 839.

(With BLACKIE, J. J.) Alkaloids of Senecio. Part II. Senecionine and squalidine. *J. Chem. Soc.*, p. 743.

(With FRAENKEL-CONRAT, H. L.) Alkaloids from Solanum pseudocapsicum. *J. Chem. Soc.*, p. 1537.

1937

Alkaloids of ergot. *Analyst*, **62**, 340.

(With BLACKIE, J. J.) Alkaloids of Senecio. III. Jacobine, jacodine and jaconine. *J. Chem. Soc.*, p. 584.

(With MARTIN, W. F. and MITCHELL, W.) Minor alkaloids of Duboisia myoporoides. *J. Chem. Soc.*, p. 1820.

(With ROBINSON, R. and URUSHIBARA, T.) Synthetical experiments relating to Carpaine. Part I. Synthesis of a basic long-chain lactone. *J. Chem. Soc.*, p. 714.

(With ROBINSON, R. and SHORT, W. F.) Synthetical experiments relating to Carpaine. Part II. *J. Chem. Soc.*, p. 715.

(With ROBINSON, R. and SMITH, L. H.) Synthetical experiments

relating to Carpaine. Part III. Some derivatives of tetrahydrofuran and intermediates of the aliphatic series. *J. Chem. Soc.*, p. 718.

(With ROBINSON, R. and WORK, T. S.) Constitution of Carpaine. III. *J. Chem. Soc.*, p. 711.

1938

The alkaloids of ergot. *Handb. exp. Pharmak.*, Ergänzwk, 6.

Chemistry and biochemistry of the alkaloids related to tryptophan. *Bull. Soc. Chim. biol.*, **20**, 685.

(With DYER, E.) Synthesis of polycyclic indoles. *J. Amer. Chem. Soc.*, **60**, 2414.

(With JACOB, A. and MADINAVEITIA, J.) Calycanthidine, a new simple indole alkaloid. *Rec. Trav. chim.*, **57**, 548.

(With MARTIN, W. F. and MITCHELL, W.) Minor alkaloids of Duboisia myoporoides. II. Poroidine and isoporoidine. *J. Chem. Soc.*, p. 1685.

1939

(With MADINAVEITIA, J. and STREULI, P.) Calycanthine. *J. Chem. Soc.*, p. 510.

(With SARGENT, L. J.) The alkaloids of Artabotrys suaveoleus. *J. Chem. Soc.*, p. 991.

(With WEITNAUER, G.) Konstitution und Synthese des Alkaloids Anonain. *Helv. chim. Acta*, **22**, 1036.